in the PBSC product, we used a combination of CD34+ selection and ex vivo incubation with anti-CD3 antibody, which resulted in a mean 5.2-log reduction of T cells (range, 4.7–6.3 log). The final PBSC products contained a mean of 9.94 (range, 4.8–13.0) $\times 10^6$ CD34+ cells/kg and 1.34 (range, 0.06–4.54) $\times 10^3$ CD3+ cells/kg. The daily dose of CY was 200 mg/m^2 in the first 3 patients and 400 mg/m^2 in the next 2 patients. The mean half-life ($t_{1/2}$) of CD3+ cells in these patients was biphasic: 0.8 days from day −7 to day −5 and 0.2 days from day −5 to day −3, correlating with ATG administration. In contrast, the mean $t_{1/2}$ of CD3+ cells was 2.5 days in patients with hematologic malignancies receiving a myeloablative preparative regimen of CY, busulfan, and etoposide. After PBSCT, the median nadirs of WBC, ANC, and platelets were 1.2 (range, 0.4–2.0), 0.9 (range, 0.1–1.7) and 135 (range, 114–185) $\times 10^9$/L, respectively. All patients are alive at a median of 8.5+ months (range, 6.9+ to 17.5+ months) after PBSCT. Compared with pre-PBSCT levels, Rodnan total skin score (TSS) decreased by 4, 10, 11, and 15 points, respectively, in 4 patients and increased by 8 points in 1 patient, who also developed SSc renal crisis requiring hemodialysis at 12 months after PBSCT. Of 4 patients with improved TSS, 1 has worsening polymyositis and 1 has recurrence of palpable tendon friction rubs. Even at the lowest CY dose, this immunosuppressive regimen provides significantly greater and more rapid T-cell kill than a conventional myeloablative regimen. The efficacy of this regimen and TCD PBSCT in SSc is encouraging. but requires longer follow-up and experience with a larger number of patients.

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CONSOLIDATION AND MOBILIZATION OF PERIPHERAL BLOOD STEM CELLS USING HIGH-DOSE CYTARABINE AND ETOPOSIDE IN ACUTE MYELOID LEUKEMIA: A SINGLE INSTITUTIONAL EXPERIENCE

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Autologous hematopoietic stem cell transplantation (autoHSCT) as consolidation in first complete remission (CR1) is an option for patients with AML. Achieving adequate numbers of stem cells and eradicating residual leukemia cells with acceptable toxicity represent two conflicting goals. Between May 2000 and May 2004, we performed autoHSCT in 24 AML patients using a reduced dose modification of a cytarabine/etoposide regimen reported by Linker (BBMT 6:50–57, 2000) as a consolidation and stem cell mobilization regimen. Median age at the time of HSCT was 59 (range, 21–73; 50% > 60 years). Most patients had intermediate-risk (63%) or high-risk cytogenetics (25%). All patients but 1 were in CR1 before autoHSCT. After induction chemotherapy, 12 patients proceeded to consolidation/mobilization. Twleve patients had additional consolidation with cytarabine-based regimens (8 with 1 consolidation and 4 with 2 consolidations). All patients then received etoposide (5 mg/kg IV every 12 hours) and cytarabine (2 g/m^2 IV every 12 hours) for 3 days instead of the 4 days described by Linker. Patients received G-CSF (10 μg/kg SC) on day 14 until the WBC count was >10,000. The median number of CD34+ stem cells collected was 5.9 $\times 10^6$/kg (range, 1.3–75.5). Some 92% of patients received busulfan and cyclophosphamide as a conditioning regimen. There were no treatment-related deaths. Engraftment was rapid: WBC ≥ 1000 in 11.5 days (range, 9–19 days), ANC ≥ 500 in 12 days (range, 10–21 days), and platelets ≥ 50,000 in 17 days (range, 11–214 days). Median follow-up is 13.6 months (range, 2–52 months). Eleven patients (46%) relapsed at a median of 5.4 months (range 1.2–27.5 months). Median disease-free survival (DFS) for all patients is 27.5 months. Patients with intermediate- and high-risk cytogenetics had a 1-year DFS of 54% and 50%, respectively. Patients receiving at least 1 consolidation before the mobilization regimen had 1-year DFS and overall survival (OS) of 56% and 73%, respectively compared with 46% and 64% for those proceeding directly from induction to mobilization. Our data suggest that autoHSCT using reduced doses of cytarabine and etoposide as a consolidation and mobilization regimen is safe and effective at achieving engraftment, and is associated with encouraging outcomes in patients with intermediate- to high-risk cytogenetics. At least 1 consolidation before the mobilization/consolidation regimen may be associated with superior outcome. Prospective trials with larger numbers of patients are needed to validate our preliminary findings.

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AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) FOR HIGH-RISK PEDIATRIC SOLID TUMORS

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Aim: The purpose of this study was to determine the toxicity of treatment with high-dose alkylating agents followed by ASCT, to monitor treatment response and to promote disease free survival in a group of pediatric patients with high risk solid tumors. **Methods:** A total of 36 patients with solid tumors having disseminated disease at diagnosis or following relapse were treated on 2 consecutive autologous transplantation protocols at the University of Minnesota between May 1995 and March 2004. Preliminary data on 11 of these patients have already been reported. The age range of the patients was 2–26 years. Of the 36 patients, 20 had a diagnosis of a Ewing's family tumor (16 Ewing's sarcoma and 4 desmoplastic small round cell tumor). Other diagnoses included rhabdomyosarcoma (in 3 patients), Wilm's tumor (in 2), medulloblastoma (in 2), and ependymoma, atypical teratoid rhabdoid tumor, glioblastoma multiforme, osteosarcoma, hepatoblastoma, retinoblastoma, cervical chordoma, ovarian small cell carcinoma and ovarian mixed anaplastic germ cell tumor each in 1 patient. Patients were eligible for transplantation if they had a complete response (CR) (18 patients) or a very good partial response with nonprogressive disease (18 patients). Conditioning therapy consisted of either oral busulfan (12 mg/kg) or intravenous busulfan (9.6 mg/kg > 4 years; 12 mg/kg < 4 years), melphalan (100 mg/m^2) and thiotepa (500 mg/m^2). Thirteen patients received the chemoprotectant amifostine. All patients received G-CSF until neutrophil engraftment. Twenty patients received PBSC, 15 patients received autologous bone marrow, and 1 patient received syngeneic marrow. **Results:** Median time to neutrophil engraftment, defined as the first of 3 consecutive days of an ANC > 0.5 $\times 10^9$/L, was 11 days (range, 9–56 days). Overall survival was 63% (range, 47%-79%) at 1 year and 33% (range, 16%-50%) at 3 years. Disease-free survival was 28% (range, 13%-43%) at 3 years. Median follow-up among survivors is 3.5 years (range, 0.6–7.9 years). Three-year overall survival for Ewing's family tumors was significantly better than for all other diagnoses (54% vs 13%; $P = .03$). Three-year overall survival was significantly better for those patients transplanted after CR (48% vs 12%; $P = .03$). There were 2 toxic deaths attributed to veno-occlusive disease. **Conclusions:** Our data indicate that ASCT after high-dose alkylating agent therapy has acceptable toxicity and should be considered as consolidation therapy for patients with high-risk Ewing's family tumors. The effectiveness of this therapy for other diagnoses appears to be limited.

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TANDEM AUTOGRAFTS FOR MULTIPLE MYELOMA PATIENTS USING TWO DIFFERENT CONDITIONING REGIMENS: AN INTERIM ANALYSIS

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Autologous stem cell transplantation (ASCT) has become a standard therapy for multiple myeloma (MM) patients. In the current study, we evaluated the toxicity and efficacy of tandem autografts

for MM patients using non–melphalan-based conditioning regimens. Patients were enrolled in the study after exhibiting response to induction therapy and meeting eligibility criteria. The treatment plan was designed to harvest a dose of 10×10^6 peripheral blood CD34+ cells/kg for the planned 2 transplants; however, a second ASCT would be pursued only in the event that CR/VGPR was not achieved after the first ASCT. The conditioning regimen for the first ASCT included oral busulfan 0.75 mg/kg every 6 hours on days −8 through −5, intravenous (IV) etoposide 10 mg/kg/day on days −4 to −2, and cyclosphosphamide (CP) IV 60 mg/kg/day on days on −3 and −2. The conditioning regimen for the second ASCT included 96-hour (days −6 through −3) continuous infusion of CP (6 g/m^2) and total body irradiation of 600 cGy in 4 fractions (days −2 and −1), followed by reinfusion of stem cell product. Forty evaluable patients have been analyzed. The median patient age was 56 years, with a median time from diagnosis to first ASCT of 8.7 months. Thirteen patients met the criteria for high-risk myeloma. After the first ASCT, 15 patients had CR/VGPR, 11 proceeded to the second ASCT, 8 refused to proceed to the second ASCT, and 6 others did not proceed for other reasons. All patients were offered posttransplantation maintenance therapy and treated with monthly bisphosphonate. There was no treatment-related mortality. Overall, 2 of 29 patients who underwent single transplantation died 17 and 15 months after the transplantation secondary to disease progression (DP) or pneumonia. Three out of 11 patients who underwent tandem transplantations died, 2 of DP at 15 and 26 months after the second transplantation, and 1 patient with a history of gastric bypass died of cryptogenic cirrhosis/liver failure at 7 months. The median time between the two ASCTs was 107 days. Improvement in response category occurred in 34% after the first ASCT and in a total of 55% after the second ASCT. The overall CR/VGPR rate was 20% before ASCT, 52% after single transplantation, and 64% after double transplantation. At a median follow-up of 15 months from the last ASCT, PFS was 14 months after single transplantation (n = 29) and 23 months after double transplantation (n = 11) (P = .46). The overall survival has not been reached for both groups. The median PFS was 41 months for all those with CR/VGPR, versus 26 months for all others (P = .0146). In conclusion, non–melphalan-based conditioning regimens seem to be effective and safe.

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CD34+CD38− AND CD34+HLA−DR− CONTENTS IN BMSC GRAFTS CORRELATE WITH SHORT-TERM ENGRAFTMENT BUT HAVE NO INFLUENCE ON LONG-TERM HEMATOPOIETIC RECOVERY IN PATIENTS WHO RECEIVED AUTOLOGOUS BONE MARROW TRANSPLANTATION

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Previous animal and human studies have demonstrated that the number of CD34+ subsets such as CD34+CD38− and CD34+HLA−DR− subsets in stem cell grafts is significantly associated with the speed of short-term hematopoietic reconstruction (SHR). The aim of this study was to determine whether these CD34+ subsets predict long-term hematopoietic reconstitution (LHR) in recipients of autologous bone marrow transplantation (ABMT).

We have examined 53 lymphoma patients who received ABMTs to determine if total mononuclear cell dose, CFU-GM, CD34+ cell dose and CD34+ cell subsets (CD34+CD38− and CD34+HLA−DR−) correlate with both SHR and LHR. Time to neutrophil engraftment (TNE) and time to platelet engraftment (TPE) were used to measure SHR, and platelet count was used as an indicator of LHR at day 100 and 1 year post-ABMT. A total of 42 and 38 patients were analyzed at day 100 and 1 year post-transplant, respectively. Patients were excluded either because they were deceased or there was lack of follow-up data. Using a univariate unadjusted logistic regression analysis, all of the predictor variables were significantly associated with SHR. However, at day 100, only CFU-GM and CD34+ cell dose significantly predicted LHR. In addition, at 1 year post-ABMT, only CD34+ cell dose predicted LHR. CD34+ cell dose maintained its significance in multivariate analysis adjusting for age, sex, and disease. None of the CD34+ cell subsets predicted LHR.

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ELEVATED MEAN CORPUSCULAR VOLUME (MCV) FOLLOWING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION: INCIDENCE AND SIGNIFICANCE

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Background: A relationship between macrocytosis and the risk of secondary leukemia has been suggested in long-term cancer survivors after chemotherapy. The incidence and significance of MCV elevation after high-dose chemotherapy and autologous hematopoietic stem cell transplantation (ASCT) is unknown. **Methods:** A retrospective analysis of 130 consecutive patients who underwent ASCT between January 1999 and December 2003 was performed. Complete blood count profile was analyzed at transplantation and then at 6 months, 1 year, and yearly after transplantation. Patients with relapse of disease within 6 months of transplantation were excluded. Sixty-three of 130 (48%) patients were eligible for the study. Patient characteristics and time to achieve long-term hematologic recovery (hemoglobin > 12 g/dL, WBC > 4000/mm^3, platelets > 150,000/mm^3) were analyzed. When available, history of alcohol abuse, abnormal liver function, thyroid function, vitamin B_{12}, and folate deficiency were recorded. **Results:** At median follow-up of 22 months (range, 6–58 months), 33 of 63 (52.8%) patients displayed elevated MCV 6 months posttransplantation. The median patients age was 12 years (range, 1–76 years). Four patients underwent double transplantation. Median time to engraftment for neutrophils and platelets was 12 and 19 days, respectively. The median time to trilineage hematologic normalcy was 289 days; 27 of 33 (81%) patients had suboptimal long-term hematopoietic recovery at 6 months (WBC, 5 months; hemoglobin, 14 months; platelets, 22 months).

At 6 months posttransplantation, 15 of 43 (35%) adult patients displayed elevated MCV (normal, 81–99 fl); the mean pretransplantation MCV of 97.5 fl increased to 102.7 fl (P = .004). Of the 20 pediatric patients, 18 (91%) displayed elevated MCV at 6 months posttransplantation; mean pretransplantation MCV of 90.8 fl increased to 94.1 fl (P = .001). Persistent MCV elevation was observed in 17 of 26 patients (65%) at 1 years posttransplantation and in 7 of 14 patients (50%) at 2 years posttransplantation. Pretransplantation red cell distribution width (RDW) was higher pretransplantation (63%) than at 6 months posttransplantation (45%). Further investigations of MCV elevation available in 10 patients were negative. No patients developed MDS or leukemia. **Conclusion:** MCV elevation after high-dose chemotherapy and ASCT is frequent, with an incidence of 52.8%. Macrocytosis occurred unrelated to anemia; routine workup of macrocytosis is unnecessary. Longer follow-up is needed to determine its significance, if any.

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MYELOABLATIVE CHEMOTHERAPY AND AUTOLOGOUS PERIPHERAL STEM CELL TRANSPLANTATION WITHOUT THE USE OF BLOOD PRODUCTS

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Background: Refusal of blood products poses a treatment challenge for Jehovah's Witness patients whose malignant diseases require high dose chemotherapy. We report our findings from a series of Jehovah's Witness patients who were enrolled in our